DOCKET NO.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: BRUCE D. WEINTRAUB, ET AL. ART UNIT: 1646

SERIAL NO.: 09/519,728 EXAMINER: LAZAR WESLEY, E.

FILING DATE: MARCH 3, 2000

FOR: MUTANTS OF THYROID STIMULATING HORMONE AND METHODS BASED THEREON

DECLARATION UNDER 37 C.F.R. § 1.132

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

I, Mariusz W. Szkudlinski, do hereby declare and state that:

1. I am one of the inventors of the subject matter claimed in the above-identified application, and one of the inventors named in the above-identified application.

2. I am a co-author of the publication entitled "Progress in understanding structure-function relationships of human thyroid-stimulating hormone", which published in Current Opinion in Endocrinology and Diabetes in 1997.

3. The work described in the article entitled "Progress in understanding structure-function relationships of human thyroid-stimulating hormone" reflects the invention of myself and Dr. Bruce D. Weintraub.

4. Mr. Mathis Grossmann was listed as a co-author in the above-mentioned article as is conventional when an individual contributes to the experimentation set forth in an article or other publication. Mr. Grossmann worked under the supervision and direction of myself and Dr. Weintraub and did not inventively contribute to the claimed features of the present invention.

5. Dr. Weintraub and I conceived of a mutant TSH heterodimer that includes (a) a TSH β subunit joined via a peptide bond at its carboxyl terminus to the amino terminus of the carboxyl terminal extension peptide of human chorionic gonadotropin and (b) an α subunit, where at least

the TSH β subunit or the TSH α subunit contains at least one amino acid substitution, where the amino acid substitution is selected from amino acid residues 11-21 of the amino acid sequence of human α subunit and/or the amino acid substitution is in amino acid residues selected from positions 58-69 of the amino acid sequence of TSH β subunit, and where the bioactivity of the mutant TSH heterodimer is greater than the bioactivity of wild type TSH heterodimer. In the course of reduction to practice of the invention, Mr. Grossmann provided information at our direction.

All statements made herein of my own knowledge are true and all statements made on information and belief are believed true. Further, I am aware that willful false statements and the like are punishable by fine, imprisonment or both, 18 U.S.C. § 1001, and that such willful false statements may jeopardize the validity of the above-captioned patent application, and any patent to issue thereon.

DATE: 05/29/02

Mariusz W. Szkudlinski

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1. I am one of the inventors of the subject matter claimed in the above-identified application, and one of the inventors named in the above-identified application.

2. I am a co-author of the publication entitled "Human Thyroid-stimulating Hormone (hTSH) Subunit Gene Fusion Produces hTSH with Increased Stability and Serum Half-life and Compensates for Mutagenesis-induced Defects in Subunit Association", which published in the Journal of Biological Chemistry in August 22, 1997.

3. The work described in the article entitled "Human Thyroid-stimulating Hormone (hTSH) Subunit Gene Fusion Produces hTSH with Increased Stability and Serum Half-life and Compensates for Mutagenesis-induced Defects in Subunit Association" represents the invention of myself and Dr. Bruce D. Weintraub.

4. Mr. Mathis Grossmann and Ms. Rosemary Wong were listed as co-authors in the above-mentioned article as is conventional when an individual contributes to the experimentation set forth in an article or other publication. Mr. Grossmann and Ms. Wong worked under the supervision and direction of myself and Dr. Weintraub and did not inventively contribute to the claimed features of the present invention.

5. Dr. Weintraub and I conceived of a mutant TSH heterodimer that includes (a) a TSH β subunit joined via a peptide bond at its carboxyl terminus to the amino terminus of the carboxyl terminal extension peptide of human chorionic gonadotropin and (b) an α subunit, where at least the TSH β subunit or the TSH α subunit contains at least one amino acid substitution, where the amino acid substitution is selected from amino acid residues 11-21 of the amino acid sequence of human α subunit and/or the amino acid substitution is in amino acid residues selected from positions 58-69 of the amino acid sequence of TSH β subunit, and where the bioactivity of the mutant TSH heterodimer is greater than the bioactivity of wild type TSH heterodimer. In the course of reduction to practice of the invention, Mr. Grossmann and Ms. Wong provided information at our direction.

All statements made herein of my own knowledge are true and all statements made on information and belief are believed true. Further, I am aware that willful false statements and the like are punishable by fine, imprisonment or both, 18 U.S.C. § 1001, and that such willful false statements may jeopardize the validity of the above-captioned patent application, and any patent to issue thereon.

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Mariusz W. Szkudlinski